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Activated T Cells and Cytokines in Bronchoalveolar Lavages from Patients with Various Lung Diseases Associated with Eosinophilia

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Increasing evidence suggests an important role for cytokines in the regulation of eosinophilic inflammation. In the present study we investigated the distribution of leukocytes, lymphocyte subsets, their activation state, and the cytokine profile present in BAL fluid from patients with various lung diseases associated with eosinophilia. For this purpose, we analyzed the levels of IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-8, GM-CSF, TNF- α , and IFN- γ , as well as soluble IL-2 and TNF receptors, in concentrated bronchoalveolar lavage (BAL) fluid obtained from clearly defined patients with allergic and nonallergic asthma, eosinophilic pneumonia, allergic bronchopulmonary aspergillosis (ABPA), hypersensitivity pneumonitis, and idiopathic pulmonary fibrosis. BAL fluid from normal individuals and sarcoidosis patients was analyzed as noneosinophilic controls. BAL cytokine levels were compared with the cellular infiltrate and the activation state of CD4 $^{+}$ and CD8 $^{+}$ T cells as measured by the expression of IL-2 receptors (CD25), HLA-DR, and the very late activation antigen VLA-1. Beside the characteristic leukocyte infiltrate in the various lung diseases, all patients demonstrated significantly increased numbers of activated CD4 and CD8 T cells compared with normal individuals. The analysis of the cytokine profile present in BAL fluid revealed a T helper type 2 (Th2) cell cytokine pattern, with elevated IL-4 and IL-5 but normal levels of IL-2 or IFN- γ in allergic asthma. ABPA patients demonstrated significantly increased levels of IL-4 and IL-5, with low but significantly elevated concentrations of IL-2 and IFN- γ . In contrast, the analysis of the cytokine profile in sarcoidosis patients revealed a Th1 cell cytokine pattern characterized by increased concentrations of IL-2 and IFN- γ but normal levels of IL-4 or IL-5. All other patient groups showed a cytokine pattern incompatible with a pure Th1 or Th2 cell response, because IL-5, IL-2, and IFN- γ were found to be significantly increased. The BAL fluid analysis of the other, mainly non-T cell-derived cytokines and soluble receptors showed increased levels in all patients compared with normal individuals and may represent the ongoing inflammatory responses. In conclusion, whereas increased IL-4 levels were found only in diseases characterized by increased IgE production, IL-5 was elevated in all patients with increased numbers of eosinophils. The close correlation between IL-5 levels, number of eosinophils, and activated T cells further supports a role for IL-5 in causing tissue eosinophilia. Walker C, Bauer W, Braun RK, Menz G, Braun P, Schwarz F, Hansel TT, Villiger B. Activated T cells and cytokines in bronchoalveolar lavages from patients with various lung diseases associated with eosinophilia. *Am J Respir Crit Care Med* 1994;150:1038-48.

Eosinophilia of the blood, airway secretion, and pulmonary tissue is a characteristic abnormality in asthma, pulmonary granulomatosis, and vasculitis, some of the interstitial lung disorders, parasitic infections involving the lungs, and most of the primary and secondary systemic eosinophilic syndromes (1-9). Eosinophils are beneficial in immune defense against helminths, in wound healing, and possibly in combating certain tumors. In recent years, however, much interest has centered on the harmful inflamma-

tory role of eosinophils in allergic and asthmatic disease (1-3, 9). Eosinophils are potent proinflammatory cells because of the release of toxic granule proteins, production of reactive oxygen species, generation of lipid mediators, such as platelet-activating factor and leukotriene C $_4$, and participation in antibody-dependent cytotoxicity reactions and thus are capable of degrading pulmonary connective tissue matrix and of injuring lung cells by specific cytotoxic actions, which are preferentially to airway epithelial cells. More recently, the potential for eosinophils to participate within cell networks as immunomodulatory cells has been recognized: eosinophils are capable of both responding to cytokines and themselves producing cytokines (9).

Asthma is now recognized as an inflammatory disorder of the airways and has been referred to as chronic eosinophilic bronchitis (1-3). There is evidence that activation of selected T cell

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